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Response to Advisory Action dated September 2, 2003

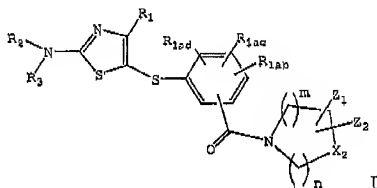
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-6 (Canceled).

Claim 7 (Currently amended). A compound of formula I



diastereomers, enantiomers or salts thereof

where

R₁ is hydrogen or R₆;

R_{1ab} and R_{1aa} are independently hydrogen, R₆ or -OR₆;

R_{1ad} is hydrogen;

one of R₂ or R₃ is hydrogen or alkyl and the other R₂ or R₃ is -Z₄-R_{6a}, where: Z₄ is -Z₁₁-C(O)-Z₁₂- and R_{6a} is phenyl substituted with Z₃;

R₆ is alkyl;

R₁, R_{1ab}, R_{1aa} and R_{1ad} are independently

(1) — hydrogen or R₆;

(2) — OH or -OR₆;

(2) — SH or -SR₆;

(4) — C(O)_qH, C(O)_qR₆, or -O-C(O)_qR₆, where q is 1 or 2;

(5) — SO₃H or -S(O)_qR₆;

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- (6) —halo;
- (7) —cyano;
- (8) —nitro;
- (9) — $Z_{14}-NR_7R_{37}$;
- (10) — $Z_4-N(R_9)-Z_3-NR_{10}R_{117}$;
- (11) — $Z_4-N(R_{12})-Z_5-R_{67}$ or
- (12) — $P(O)(OR_{67})_2$;

R_2 and R_3 are each independently H, Z_4-R_{68} or $Z_4-NR_{74}R_{86}$;

R_5 , R_{68} and R_{69} are independently alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_{17} , Z_2 and one or more groups Z_{25} ;

R_{70} , R_{86} , R_9 , R_{10} , R_{11} and R_{12}

- (1) are each independently hydrogen, or Z_4R_{68} ; or
- (2) R_{70} and R_{86} may together be allylene, alkenylene, or heteroalkylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_{17} , Z_2 and one or more groups Z_{25} or
- (3) any two of R_9 , R_{10} and R_{11} may together be allylene, alkenylene or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_{17} , Z_2 and Z_{25} ;

X_2 is CZ_{38} , NZ_{38} , O or S;

Z_{3a} is $-C(O)_qZ_{6a}$, where q is 1, H, hydroxy, optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted aryl, optionally substituted aralkyl, OZ_6 , $C(O)_qH$, $-C(O)_qZ_{6a}-Z_4-NZ_7Z_8$, or $-Z_4-N(Z_{10})-Z_5-Z_6$;

n is 1 to 3 2;

m is zero to 2 1;

Z_1 and Z_2 are hydrogen;

Z_0 is $-Z_4-NZ_7Z_8$, where Z_4 is alkyl;

Z_{17} , Z_2 and Z_3 are each independently

- (1) —hydrogen or Z_{67} ;

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(2) —OH or —OZ₆₇(3) —SH or —SZ₆₇(4) —C(O)_qH₃—C(O)_qZ₆₇ or —O—C(O)_qZ₆₇, where q is 1 or 2;(5) —SO₂H₃—S(O)_qZ₆₇ or S(O)_qN(Z₆₇)Z₆₇

(6) —halo;

(7) —cyano;

(8) —nitro;

(9) —Z₄—NZ₇Z₈₇(10) —Z₁₄—N(Z₉)—Z₅—NZ₆Z₈₇(11) —Z₁₄—N(Z₁₀)—Z₅—Z₆₇(12) —Z₄—N(Z₁₀)—Z₅—I₃

(13) —oxo;

(14) —any two of Z₁₄, Z₂₃, and Z₃ on a given substituent may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or(15) —any two of Z₁₄, Z₂₃, and Z₃ on a given substituent may together be —O—(CH₂)_q—O—;Z₄ and Z₅ are each independently

(1) —a single bond;

(2) —Z₁₄—S(O)_q—Z₁₂₇(3) —Z₁₄—C(O)—Z₁₂₇(4) —Z₁₄—C(S)—Z₁₂₇(5) —Z₁₄—O—Z₁₂₇(6) —Z₁₄—S—Z₁₂₇(7) —Z₁₄—O—C(O)—Z₁₂₇(8) —Z₁₄—C(O)—O—Z₁₂₇ or

(9) —alkyl

Z₆ and Z₆₇ is alkyl; are independently

(i) —alkyl, hydroxyalkyl, alkoxyalkyl, alkonyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl;

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- (ii) ~~a group (i) which is itself substituted by one or more of the same or different groups (i);~~
 or
 (iii) ~~a group (i) or (ii) which is independently substituted by one or more of the groups (2) to (15) of the definition of Z₄;~~

Z₇ and Z₈ are each independently hydrogen or -Z₄-Z_{6a}, where Z₄ is a single bond.

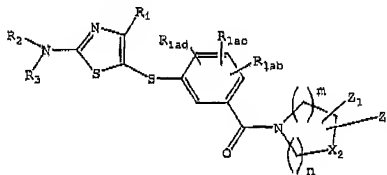
Z₇, Z₈, Z₉ and Z₁₀

- (1) ~~are each independently hydrogen or -Z₄-Z_{6a};~~
 (2) ~~Z₇ and Z₈ may together be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z₁, Z₂ and Z₃, or~~
 (3) ~~Z₇ or Z₈, together with Z₉, may be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z₁, Z₂ and Z₃;~~

Z₁₁ and Z₁₂ are each independently a single bond.

- (1) ~~a single bond;~~
 (2) ~~alkylene;~~
 (3) ~~alkenylene, or~~
 (4) ~~alkynylene;~~

Claim 8 (Previously presented). A compound of claim 7 having the formula



Claim 9 (Currently amended). A compound of claim 8 where

R₂ is hydrogen or alkyl; and

R₃ is -Z₄R_{6a}, where: Z₄ is -C(O)- and R_{6a} is phenyl substituted with Z₃.

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(a) Z_4 is a single bond and R_{4a} is heteroaryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;

(b) Z_4 is $-C(O)-$ and R_{4a} is

(1) aryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;

(2) alkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;

(3) cycloalkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or

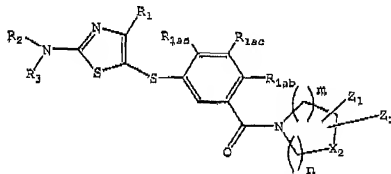
(4) heterocyclo optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or

(c) Z_4 is $-C(O)-O-$ and R_{4a} is alkyl, cycloalkyl, aryl or aralkyl, any of which may be optionally substituted with one or more Z_1 , Z_2 or Z_3 .

Claim 10 (Currently amended). A compound of claim 9 wherein R_{1ab} [[.]] and R_{1ac} and R_{1ad} are independently H[[.]] or alkyl, hydroxy, nitro, halo, $-OR_6$, $-NR_2R_6$, $-C(O)_qH$ or $-C(O)_qR_6$.

Claim 11 (Original). A compound of claim 10 wherein R_{1ab} and R_{1ac} are independently alkyl.

Claim 12 (Currently amended). A compound of claim 8 having the following formula



where one of R_{1ab} [[.]] and R_{1ac} and R_{1ad} is H and the other is alkyl or $-OR_6$ two are independently alkyl, hydroxy, nitro, halo, $-OR_6$, $-NR_2R_6$, $-C(O)_qH$ or $-C(O)_qR_6$.

Claim 13 (Currently amended). A compound of claim 12 wherein one of R_{1ab} [[.]] and R_{1ac} and R_{1ad} is H and the other is two are independently alkyl or $-OR_6$.

Claim 14 (Previously presented). A compound of claim 13 wherein R_{1ac} is H.

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Claim 15 (Canceled).

Claim 16 (Canceled)

Claim 17 (Previously presented). A pharmaceutical composition comprising at least one compound of claim 7 and a pharmaceutically acceptable vehicle or carrier therefor.

Claim 18 (Original). A pharmaceutical composition of claim 17 further comprising at least one additional therapeutic agent selected from anti-inflammatory agents, anti-proliferative agents, anti-cancer agents or anti-cytotoxic agents.

Claim 19 (Original). A pharmaceutical composition of claim 18 wherein the additional therapeutic agents are selected from steroids, mycophenolate mofetil, LTD₄ inhibitors, CTLA4-Ig, LEA-29Y, phosphodiesterase inhibitors, antihistamines, or p³⁸ MAPK inhibitors.

Claim 20 (Withdrawn). A method of treating a Tec family tyrosine kinase-associated disorder comprising the step of administering to a patient in need thereof, an effective amount of at least one compound of claim 1.

Claim 21 (Withdrawn). The method of claim 20 wherein the Tec family tyrosine kinase-associated disorder is an Emt-associated disorder,

Claim 22 (Withdrawn). The method of claim 21 wherein the Emt-associated disorder is selected from transplant rejection, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, lupus, graft vs. host disease, T-cell mediated hypersensitivity disease, psoriasis, Hashimoto's thyroiditis, Guillain-Barre syndrome, cancer, contact dermatitis, allergic disease, asthma, ischemic or reperfusion injury, atopic dermatitis, allergic rhinitis, or chronic obstructive pulmonary disease.

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Claim 23 (New). A method of treating a Tec family tyrosine kinase-associated disorder comprising the step of administering to a patient in need thereof, an effective amount of at least one compound of claim 7.

Claim 24 (New). The method of claim 23 wherein the Tec family tyrosine kinase-associated disorder is an Emt-associated disorder.

Claim 25 (New). The method of claim 24 wherein the Emt-associated disorder is selected from transplant rejection, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, lupus, graft vs. host disease, T-cell mediated hypersensitivity disease, psoriasis, Hashimoto's thyroiditis, Guillain-Barre syndrome, cancer, contact dermatitis, allergic disease, asthma, ischemic or reperfusion injury, atopic dermatitis, allergic rhinitis, or chronic obstructive pulmonary disease.